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(71) Applicant and
(72) Inventor: **CREDE, Helfried, Hans, Rudolf** [DE/ZA]; 12 Seaview Road, 7130 Somerset West (ZA).

(74) Agents: **DONALD, HEATHER, June** et al.; Spoor & Fisher, PO Box 41312, 2024 Craighall (ZA).

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(54) Title: PHARMACEUTICAL COMPOSITION CONTAINING BLACK CUMIN OIL, FLAX OIL AND BORAGO OIL

(57) Abstract: This invention relates to an enteral pharmaceutical composition for the treatment of multiple sclerosis. The pharmaceutical composition includes black cumin oil *(nigella sativa*, flax oil *(oleium lini)*, borage oil *(borago officinalis)*, vitamins and minerals. When taken enterally, the composition has been shown to treat multiple sclerosis successfully. The dosage of the composition depends on the severity of the multiple sclerosis and the patient, but a usual dosage is 20ml to 40ml per day.

PHARMACEUTICAL COMPOSITION CONTAINING BLACK CUMIN OIL, FLAX OIL AND BORAGO OIL

BACKGROUND TO THE INVENTION

This invention relates to an enteral pharmaceutical composition for the treatment of multiple sclerosis.

Multiple sclerosis is caused by damage to the myelin sheath which covers the axons of neurons. Nerve signals travel from neuron to neuron via axons. The myelin sheath serves as an insulation against signal loss to neighbouring tissue. A damaged myelin sheath leads to a distortion or complete disappearance of signals.

In addition, the myelin sheath is sub-divided into distinct sections which are separated from each other by nodes, which are called "Nodes of Ranvier". The latter's function is to speed up the transmission of nerve signals.

Damage to the myelin sheath therefore not only distorts or leads to the complete loss of nerve signals, but also slows down their transmission from neuron to neuron.

This, in essence, is the nature of the phenomenon known as multiple sclerosis. As the damage to the myelin sheaths progresses, the patient affected by the disease loses control of essential body functions: loss of balance, slow and shaky walking patterns, speech impediment, even loss of bladder control and other symptoms.

Myelin is a very complex substance, consisting of various fats, fatty acids, phospho-lipids, proteins and even cholesterol.

The vast majority of these substances are either fat or fat derivatives. It is therefore clear that the formation and periodic regeneration of myelin depends on dietary intake and a well-functioning metabolic system.

It is believed that if a treatment could be found which repairs the damage to the myelin sheath and which would prevent the damage from re-occurring, it would either cure the sufferer or at least reduce the symptoms to bearable levels.

It is an object of the invention to provide a pharmaceutical composition, which will assist in curing the causes of multiple sclerosis

SUMMARY OF THE INVENTION

According to the invention there is provided an enteral pharmaceutical composition containing black cumin oil *(nigella sativa)*, flax oil *(oleium lini)* and borage oil *(borago officinalis)* for the treatment of multiple sclerosis.

The invention also relates to a method of treating multiple sclerosis using the aforementioned pharmaceutical composition, and to the use of black cumin oil,

flax oil and borage oil in a method of making a medicament for use in a method of treating multiple sclerosis.

The composition typically contains 70 to 80% by mass, preferably 75% by mass flax oil; 10% to 20% by mass, preferably 15% by mass black cumin oil; and 5% to 15% by mass, preferably 10% by mass borage oil.

According to a preferred embodiment of the invention there is provided an enteral pharmaceutical composition for treating multiple sclerosis, the composition containing 65% to 75% by mass polyunsaturated fatty acids wherein one of the polyunsaturated fatty acids is gamma-linolenic acid. The other polyunsaturated fatty acids may be selected from alpha-linolenic acid and linoleic acid.

Advantageously, the composition contains 1% to 10 % by mass gamma-linolenic acid.

In a preferred embodiment of the invention, the pharmaceutical composition contains, by mass of the composition:

Alpha-Linolenic Acid	40% to 50%, preferably 45%
Linoleic Acid	22% to 26%, preferably 24%
Oleic Acid	16% to 20%, preferably 18%
Gamma-Linolenic Acid	1% to 5%, preferably 2%
Palmitic Acid	4% to 7%, preferably 6%
Stearic-Acid	2% to 5%, preferably 4%
Other fatty Acids	2%
Aromatic Oils	0.3%

Preferably, the composition also contains enzymes, preferably desaturase enzymes such as delta-6-desaturase.

Advantageously, the composition also contains vitamins, preferably vitamins B3, B6 and C, and minerals, preferably zinc and magnesium.

DETAILED DESCRIPTION OF THE INVENTION

This invention relates to an enteral pharmaceutical composition for the treatment of multiple sclerosis.

The pharmaceutical composition includes black cumin oil *(nigella sativa)*, flax oil *(oleium lini)*, borage oil *(borago officinalis)* and vitamins and minerals.

Black cumin oil is composed of the following fatty acids by mass:

Myristic	0.2%
Palmitic	12.4%
Palmitoleic	0.2%
Stearic	2.7%
Oleic	23.7%
Omega 6 (Linoleic)	57.2%
Omega 3 (Linolenic)	0.2%
Arachidic	0.4%
Gadoleic	0.4%
Other	0.6%

Flax oil is composed of the following fatty acids by mass:

Omega 3 (Linolenic)	60.1%
Omega 6 (Linoleic)	15.2%
Oleic	16.4%
Palmitic	3.9%

Stearic	3.6%
Other	0.8%

Borage oil is composed of the following fatty acids by mass:

Gamma-Linolenic acid	22%
Linoleic acid	38%
Oleic acid	16%
Palmitic	9%
Gadoleic acid	4%
Stearic acid	3%
Other total	8% (palmitoleic, linolenic, arachidic, erucic, behenic, nervonic).

The flax oil, borage oil and black cumin oil are mixed at a percentage 75%, 10% and 15% by mass respectively to provide a medicinal composition according to the invention. These percentages may vary, depending on the individual's requirements.

When taken enterally the composition has been shown to treat multiple sclerosis successfully. The dosage of the composition depends on the severity of the multiple sclerosis and the patient, but a usual dosage is 20ml to 40ml per day, typically 20ml per day.

The composition of the invention provides an abundance of polyunsaturated fatty acids which are believed to be the building materials for the formation of myelin, the breakdown of which is believed to be the root cause of multiple sclerosis. This abundance of fatty acids is provided by the flax oil, the black cumin oil and the borage oil.

The conversion of essential fatty acids to substances required for the formation of myelin is a slow and inefficient process. It is assumed that only about 2 to 3

% of essential fatty acids entering the metabolic pathways are eventually converted to the substances needed, even if all factors perform normally. The process is further slowed down by various aspects, either acquired or genetically programmed, such as malfunction of the small intestine (inhibiting absorption of co-factors), liver damage (leading to, for instance, inadequate formation of enzymes) or inadequate supply and/or absorption of essential fatty acids.

The enzymes required for essential fatty acids metabolism are delta-6, delta-5 and delta-4-desaturase, of which delta-6-desaturase is the most important because if its function is impaired for whatever reasons, the other two enzymes have nothing to work with. It may also be that delta-6-desaturase is not produced by the body in sufficient quantities, which leads to the same malfunction. The borage oil contains gamma-linolenic acids, a substance normally produced in the human body by the enzyme delta-6-desaturase acting on dietary linoleic acid through a process known as desaturation and elongation. In the composition of the invention, gamma-linolenic acid is therefore available for subsequent metabolic conversions even if no or to little delta-6-desaturase is present. Borage seeds are also a source of delta-6-desaturase, thus making a basic supply of delta-6-desaturase available for the relevant conversions of fatty acids, not only into gamma-linolenic acid but also dihomo-gamma-linolenic acid, from which arachidonic acid and other essential fatty acid derivatives are formed.

Enzymes require so-called co-factors in order to properly perform their functions. In the case of delta-6, delta-5 and delta-4 -Desaturase, the co-factors are the vitamins B3, B6, and C and the minerals zinc and magnesium. Even an abundance of enzymes will not be able to effect the proper essential-fatty-acid metabolisms even if only one of the co-factors is not available in sufficient quantities. As a consequence, the complex end products of said metabolism, arachidonic acid with 4 double bonds, and docosahexaenoic

acid, with 6 double bonds, will not be available in sufficient quantities. These two fatty acids are "brain fatty acids", meaning that they are incorporated into various brain structures, playing a vital role in the formation of myelin, and the transmission of nerve signals. Multiple sclerosis sufferers are therefore not only affected by a lack of available essential fatty acids, but also by a lack of available enzymes and/or a lack of available co-factors. Borage seeds contain the enzyme delta-6-desaturase, which is therefore made available through the oil, as an oil-soluble substance and/or through seed particles which are purposely left in the oil after cold-pressing. Therefore, even if a patient is lacking the enzyme delta-6-desaturase, it is made available through the borage oil and seed component of the present invention.

Example 1

In a typical example of the invention, 750ml flax oil is mixed with 100ml of borage oil and 150ml of black cumin oil to provide a preparation which is made up by the following by mass of the composition:

Alpha-Linolenic Acid	45.5%
Linoleic Acid	23.6%
Oleic Acid	17.9%
Gamma-Linolenic A	2.2%
Palmitic Acid	5.6%
Stearic Acid	3.5%
Other fatty Acids	2.1%
Aromatic Oils	0.3%

The composition also comprised 0,1g vitamin B6, 0,1g vitamin B3, 5g vitamin C, 14g magnesium and 0,6g zinc.

Example 2

A lady in her early fifties had multiple sclerosis for "more than 10 years". Her condition had gradually worsened over time, from plateau to plateau, until she had developed the usual spectrum of MS symptoms: impaired eyesight, speech impediments, incontinence, "tight-chest" phenomena, numbness in various limbs, walking impediments, and more.

She began using the composition described in Example 1 at a dosage of 20ml per day. Her condition improved after 4 to 6 weeks. Approximately 3 months after beginning to use the composition of the invention she was practically symptom free and after 15 months she was still practically symptom free.

Example 3

A young man in his mid-20s was diagnosed to have multiple sclerosis in December 2001. His condition deteriorated rapidly, to the point where he could no longer reach out for an object in front of him without missing it. He had also, by May 2002, developed a strong speech impediment.

In May 2002, the patient started using the composition of Example 1 at a dosage of 20ml per day. Within 4 months, his condition had improved to such an extent that he was practically symptom-free.

CLAIMS

1. An enteral pharmaceutical composition containing black cumin oil *(nigella sativa)*, flax oil *(oleium lini)* and borage oil *(borago officinalis)* for the treatment of multiple sclerosis.

2. The composition according to claim 1 containing 70 to 80% by mass, flax oil; 10% to 20% by mass, black cumin oil; and 5% to 15% by mass borage oil.

3. The composition according to claim 2 containing 75% by mass, flax oil; 15% by mass, black cumin oil; and 10% by mass borage oil.

4. The use of black cumin oil *(nigella sativa)*, flax oil *(oleium lini)* and borage oil *(borago officinalis)* in a method of making a medicament for use in a method of treating multiple sclerosis.

5. The use according to claim 4, wherein the medicament contains 70 to 80% by mass, flax oil; 10% to 20% by mass, black cumin oil; and 5% to 15% by mass borage oil.

6. The use according to claim 5, wherein the medicament contains 75% by mass, flax oil; 15% by mass, black cumin oil; and 10% by mass borage oil.

7. An enteral pharmaceutical composition for treating multiple sclerosis, the composition containing 65% to 75% by mass polyunsaturated fatty acids wherein one of the polyunsaturated fatty acids is gamma-linolenic acid.

8. The composition according to claim 7, wherein the polyunsaturated fatty acids are selected from alpha-linolenic acid and linoleic acid.

9. The composition according to claim 7, containing 1% to 10 % by mass gamma-linolenic acid.

10. The composition according to claim 7, containing in percentage by mass of the composition:

Alpha-Linolenic Acid	40% to 50%
Linoleic Acid	22% to 26%
Oleic Acid	16% to 20%
Gamma-Linolenic Acid	1% to 5%
Palmitic Acid	4% to 7%
Stearic-Acid	2% to 5%
Other fatty Acids	2%
Aromatic Oils	0.3%.

11. The composition according to claim 10, containing in percentage by mass of the composition:

Alpha-Linolenic Acid	45%
Linoleic Acid	24%
Oleic Acid	18%
Gamma-Linolenic Acid	2%
Palmitic Acid	6%
Stearic-Acid	4%
Other fatty Acids	2%
Aromatic Oils	0.3%.

12. The composition according to claim 7, containing desaturase enzymes.

13. The composition according to claim 12, containing delta-6-desaturase.

14. The composition according to claim 1 or claim 7; containing vitamins B3, B6 and C, zinc and magnesium.

15. A method of treating multiple sclerosis, the method including the step of administering an enteral pharmaceutical composition containing black cumin oil *(nigella sativa)*, flax oil *(oleium lini)* and borage oil *(borago officinalis)* to a patient in need thereof.

16. The method according to claim 15, the composition containing 70 to 80% by mass, flax oil; 10% to 20% by mass, black cumin oil; and 5% to 15% by mass borage oil.

17. The method according to claim 16, the composition containing 75% by mass, flax oil; 15% by mass, black cumin oil; and 10% by mass borage oil.

18. The method according to claim 15, wherein the composition is administered to the patient at a dosage of 20ml-40ml per day.

19. The method according to claim 18, wherein the composition is administered to the patient at a dosage of 20ml per day.

INTERNATIONAL SEARCH REPORT

PCT/IB 03/03054

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K35/78 A61K31/202 A61P39/06 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, FSTA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	HARBIGE L S ET AL: "The protective effects of omega-6 fatty acids in experimental autoimmune encephalomyelitis (EAE) in relation to transforming growth factor-beta 1 (TGF-beta1) up-regulation and increased prostaglandin E2 (PGE2) production" CLINICAL AND EXPERIMENTAL IMMUNOLOGY, vol. 122, no. 3, December 2000 (2000-12), pages 445-452, XP002263545 & ISSN: 0009-9104	7
Y	page 446, column 2 page 451, column 2	1-19

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
2 December 2003	16/12/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Winger, R

INTERNATIONAL SEARCH REPORT

PCT/IB 03/03054

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X Y	EP 0 520 624 A (EFAMOL HOLDINGS) 30 December 1992 (1992-12-30) page 6, line 28; examples	7 7-14
X Y	EP 0 347 056 A (EFAMOL HOLDINGS) 20 December 1989 (1989-12-20) page 4, line 40 - line 45; examples	7 7-14
Y	TREMLETT H L ET AL: "Nonprescription medicine use in a multiple sclerosis clinic population" BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, vol. 50, no. 1, July 2000 (2000-07), pages 55-60, XP002263546 & ISSN: 0306-5251 page 59, column 2, paragraph 3	1-19
A	WO 00/32211 A (CREDE THOMAS ; CREDE HELFRIED HANS RUDOLF (ZA)) 8 June 2000 (2000-06-08) the whole document	

PCT/IB 03/03054

INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 15-19 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/IB 03/03054

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